Journal of Cranio-Maxillo-Facial Surgery 47 (2019) 826–831

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

The rare entity of cystadenocarcinoma (CAC) in parotid gland: A single-center experience

Bing Guo [a, 1], Yu-an Cao [b, 1], Xingjun Qin [a, **], Chunyue Ma [a, *]

[a] Department of Oral Maxillofacial and Head & Neck Oncology, Shanghai Ninth People's Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, 200011, China
[b] Department of Stomatology, The Second Affiliated Hospital of Soochow University, Suzhou, Jiangsu Province, 215004, China

ARTICLE INFO

Article history:
Paper received 27 November 2018
Accepted 6 February 2019
Available online 13 February 2019

Keywords:
Cystadenocarcinoma (CAC)
Parotid gland
Postoperative recurrence
Predictive factor
5-Year recurrence-free survival rate
Extremely rare entity

ABSTRACT

Purpose: Cystadenocarcinoma (CAC) is an extremely rare disease in parotid gland. This study aimed to identify the clinical characteristics of CAC, and the therapeutic options for its treatment. An attempt was also made to identify postoperative recurrence-related risk factors.
Material and methods: A retrospective study was conducted of CAC patients treated between 2008 and 2018. Predictive factors for postoperative recurrence (5-year RFS rate) were preliminarily filtered by Kaplan–Meier analysis and then further confirmed by a Cox regression model. Postoperative recurrence was defined as the primary outcome variable and was measured using both univariate and multivariate analysis.
Results: A total of 27 patients were analyzed, and the total incidence of postoperative recurrence was 33.3% (9/27). In the Cox regression analysis, patients who received a superficial parotidectomy were 0.046 times more likely to develop tumor relapse than those who only underwent enucleation ($p = 0.032$; 95% CI: 0.003–0.070). The chances of tumor recurrence in patients with the cribriform subtype were 9.701 times that for cases with a papillary pattern ($p = 0.016$; 95% CI: 1.517–62.030). The risk of postoperative recurrence increased abruptly, with an OR of 6.373 ($p = 0.042$; 95% CI: 1.070–37.965), when LN metastasis was found in patients.
Conclusion: Preoperative diagnosis of CAC in parotid gland is extremely important for allowing surgeons to apply appropriate therapeutic strategies (enucleation or superficial parotidectomy). Patients with LN metastasis, cribriform pattern, and Ki-67 positivity should be treated further to avoid tumor relapse.

1. Introduction

Papillary cystadenocarcinoma (CAC), first reported by WHO in 1991, is an extremely rare neoplasm, originally categorized into malignant cystadenoma and low-grade papillary adenocarcinoma. In 1996, scholars proposed a novel subtype termed as low-grade salivary duct carcinoma, which is a variant of CAC, i.e. low-grade, cribriform CAC. These vague concepts were in use for 14 years until WHO redefined them as CACs comprising either papillary or cribriform patterns. CAC has been extensively identified in ovary, pancreas, breast, and lung (Seifert and Sobin, 1991; Shannon et al., 2017; Doulamis et al., 2016; Koufopoulos et al., 2017), but seldom seen in oral, maxillofacial, or head and neck regions. With further developments in pathological diagnosis techniques, CAC has presented in parotid gland, sublingual gland, minor salivary gland, hard palate, tongue, and mandible, according to reports by different institutions over the past two decades (Kawahara et al., 2010; Harimaya et al., 2006; Michal et al., 2013; Giblett et al., 2017; Kokabu et al., 2015; Wanjari et al., 2014; Nakagawa et al., 2002; Takei et al., 2012; Srivanitchapoom et al., 2014). Foss et al. reported 57 cases of CAC (35 in parotid gland) through imaging of pathological features and analysis of tumor-related outcomes, but without filtering of prognosis-related risk factors (Foss et al., 1996). Since then, several case reports of CAC in parotid gland have been published. In an attempt to comprehensively analyse CAC, Cai et al. found 65 cases of CAC in salivary gland (57 in parotid gland)

* Corresponding author.
** Corresponding author.
E-mail addresses: qinxj1989@sina.com (X. Qin), maxifama@163.com (C. Ma).
[1] Contributed equally to this work.

https://doi.org/10.1016/j.jcms.2019.02.005
1010-5182/

through a population-based national registry (Surveillance, Epidemiology, and End Results — SEER), and performed statistical analysis of 5- and 10-year cause-specific/overall survival rates. Recurrence-free survival (RFS) was not included in their investigation, because of missing data on local and regional recurrence following surgical procedures (Cai et al., 2016). Our study focused on CAC in parotid gland (27 cases) in a single institution, aiming to clearly identify the clinical features and therapeutic options, in addition to finding prognostic predictors linked to tumor recurrence. To our knowledge, this is the first investigation to investigate risk factors for postsurgical recurrence of CAC in parotid gland, with the aim of providing clinical references for dealing with this rare entity.

2. Material and methods

2.1. Study design and participants

The retrospective study designed and implemented to address this clinical issue was approved by the ethics committee of our hospital. Data were collected from the files of CAC patients who received treatment in the Department of Oral, Maxillofacial and Head & Neck Oncology between 2008 and 2018. The data did not include information that could identify the patients.

The patients needed to meet the following inclusion criteria: (1) diagnosed with CAC in parotid gland; (2) received surgical treatment, including tumor enucleation, superficial parotidectomy, or total parotidectomy; (3) received treatments only in our institution; (4) with complete treatment records and follow-up information. All procedures were carried out in accordance with study guidelines and regulations.

2.2. Study variables and estimation model

The demographic and comorbidity features included age at surgical treatment, gender, and concomitant disease. CAC-related characteristics included preoperative diagnosis, primary site, course of disease, status of primary or recurrence, preoperative radiotherapy (RT) and chemotherapy (CT), and clinical manifestations (nodosities, limitation in movement, hard texture, prosopoplegia, tenderness, and tumor boundary). Treatment records included surgical treatment, lymph node (LN) metastasis, maximum diameter, TNM stage, pathological subtype, Ki-67 status, and postoperative RT and CT. All aforementioned variables were defined as primary predictive factors; the outcome variable was postoperative recurrence (PC) of CAC (5-year RFS rate). An association study of primary predictive factors with the outcome variable was performed to filter those factors with a predictive role.

2.3. Statistical analysis

Sociodemographic and clinical variables were analyzed using descriptive statistics. The association between primary predictive factors and PC was tested using Kaplan–Meier analysis (log-rank test; $p < 0.05$ was deemed statistically significant). Those primary factors were then entered into a Cox-regression analysis to eliminate the reciprocal influence and determine the final predictive role. Odds ratios, 95% confidence intervals, and p-values were recorded. Statistical analyses were performed with SPSS software (version 21.0; SPSS, Chicago, IL).

3. Results

3.1. Demographic characteristics

A total of 31 patients were diagnosed with CAC in parotid gland and underwent surgical procedures in our department from 2008 to 2018. Four cases were excluded according to the inclusion criteria; in total, 27 samples were analyzed (Fig. 1). Male patients ($n = 18$) accounted for the majority of patients, with a percentage of 66.7%. The age at surgical treatment ranged from 17 to 79 years

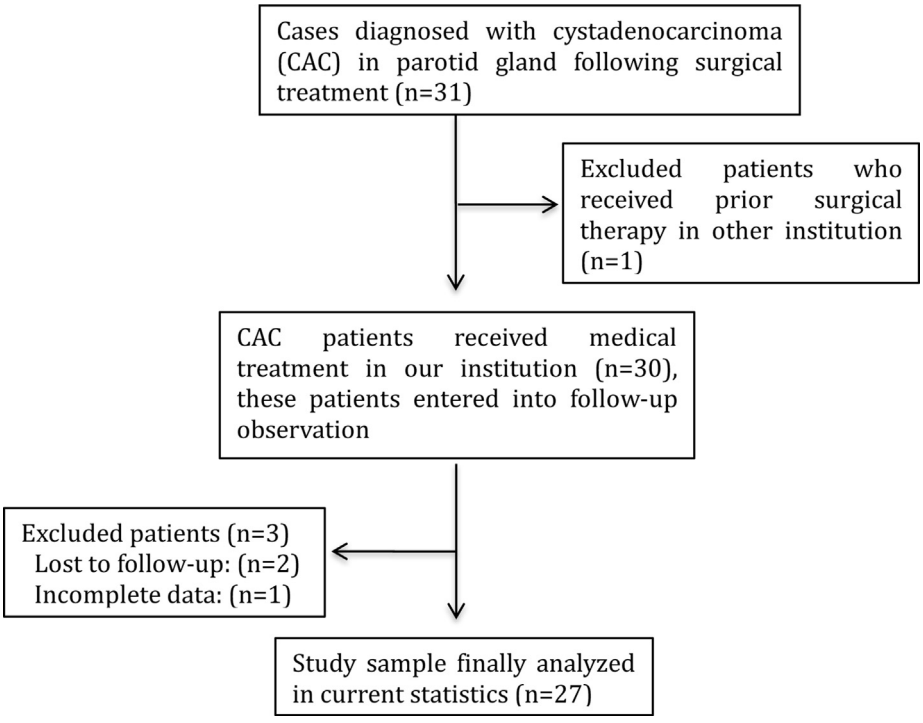

Fig. 1. Flow diagram for patient inclusion.

(mean 49.55; median 53), with 14 (51.9%) patients older than 60 years old. Systemic disease data are shown in Table 1.

3.2. Factors relating to CAC in parotid gland

All 27 patients suffered from cystadenocarcinoma in parotid gland. 15 patients (55.6%) found a painless mass in the right parotid gland, and most patients ($n = 20$; 74.1%) reported the course of the disease as being less than 2 years, indicating that this asymptomatic mass showed a relative high rate of proliferation. Because of the extremely low incidence in parotid gland, and the absence of typical symptoms, CAC can be easily misdiagnosed as benign or malignant tumors of parotid gland , in these cases as pleomorphic adenoma ($n = 16$), malignant pleomorphic adenoma ($n = 3$), basal cell adenoma ($n = 2$), acinic cell carcinoma ($n = 2$), mucoepidermoid carcinoma ($n = 2$), and even cystic hydroma ($n = 1$) (Fig. 2). The clinical manifestations of CAC were essentially similar to those of benign or malignant tumors in parotid gland. In this study, 66.7% of cases presented as a mass of nodosities, 64.9% of cases as having a hard texture, and 37.3% resulting in limitation of movement (Fig. 3). A wide range of clinical or radiological features may be found in CAC, prompting the difficulty in preoperatively definite diagnosis of this unique subtype.

3.3. Treatment-related record and postoperative recurrence

Depending on the depth of tumor location, tumor size, and biological behavior, therapeutic options comprise enucleation, superficial parotidectomy, and total parotidectomy. Due to the high incidence of misdiagnosis with CAC, enucleation or superficial parotidectomy (SP) were mostly applied, on the basis of a benign tumor misdiagnosis, and total parotidectomy (TP) was only performed in cases with poor biological behavior. In our study, 11 cases (40.7%) underwent enucleation, followed by 10 patients (37.0%) receiving SP, and six (22.2%) samples requiring TP. Simultaneous neck dissection was carried out in 10 patients, five of whom were found to have lymph node (LN) metastasis. Pathological analysis was used to diagnose the specific type of tumor. Papillary pattern was the most common subtype of CAC, with 19 cases (70.4%); the other eight cases (29.6%) were categorized as cribriform pattern. Ki-67 is a sensitive biomarker frequently used in tumor analysis for its predictive role regarding cell or tissue proliferation; its positive

Table 1
Clinical characteristics, treatment record, and prognostic factor analysis for CAC in parotid gland.

Variable	No. of cases	No. of recurrences	5-year RFS	*p*-value
Age (Yr)				
< 60	13 (48.1%)	7	40.6%	0.038
≥60	14 (51.9%)	2	90.9%	
Gender				
Female	9 (33.3%)	3	64.4%	0.952
Male	18 (66.7%)	6	63.5%	
Systemic disease				
No	17 (63.0%)	5	64.1%	0.935
Yes	10 (37.0%)	4	65.6%	
Primary site				
Left	12 (44.4%)	4	55.9%	0.826
Right	15 (55.6%)	5	69.5%	
Course of disease				
≤12 months	16 (59.3%)	5	68.5%	0.798
13–36 months	7 (25.9%)	2	71.4%	
> 36 months	4 (14.8%)	2	50.0%	
Tumor status				
Primary	23 (85.2)	7	67.2%	0.586
Recurrent	4 (14.8)	2	50.0%	
Treatment				
Tumor enucleation	11 (40.7%)	6	23.1%	0.036
Superficial parotidectomy	10 (37.0%)	2	87.5%	
Total parotidectomy	6 (22.2%)	1	83.3%	
LN metastasis				
No	22 (81.5%)	6	70.2%	0.039
Yes	5 (18.5%)	3	40.0%	
Max diameter				
< 3 cm	8 (29.6%)	2	40.0%	0.901
≥3 cm	19 (70.4%)	7	66.8%	
TNM stage				
I	6 (22.2%)	0	100%	0.245
II	12 (44.4%)	5	55.9%	
III/IV	9 (33.3%)	4	55.6%	
Pathological subtype				
Papillary	19 (70.4%)	4	78.7%	0.012
Cribriform	8 (29.6%)	5	31.3%	
Ki-67 status				
Negative	15 (55.6%)	2	81.5%	0.008
Positive	12 (44.4%)	7	43.8%	
Postoperative RT				
No	20 (74.1%)	5	74.5%	0.092
Yes	7 (25.9%)	4	35.7%	
Postoperative CT				
No	24 (88.9%)	8	64.4%	0.728
Yes	3 (11.1%)	1	66.7%	

LN: lymph node; RT: radiotherapy; CT: chemotherapy; RFS: recurrence-free survival.

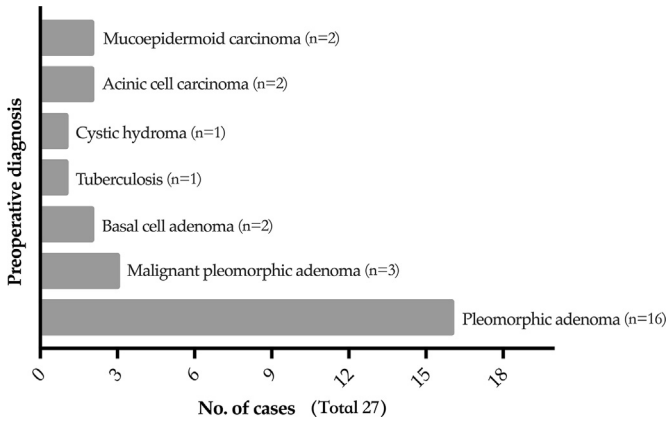

Fig. 2. Preoperative diagnosis of CAC in parotid gland.

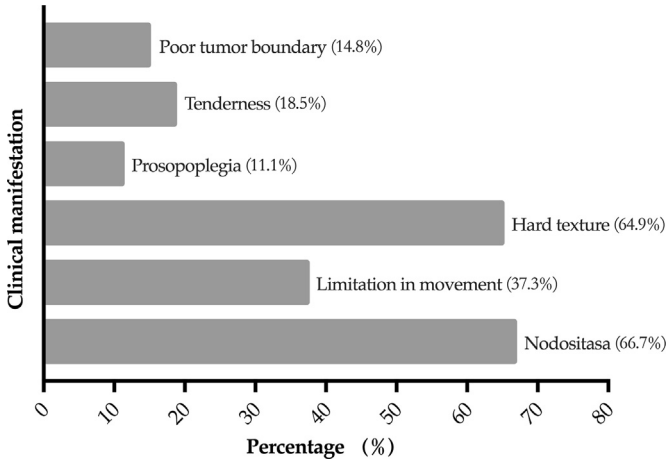

Fig. 3. Clinical manifestations of CAC in parotid gland with no specific characteristics.

ratio in CAC was about 44.4%. Based on the pathological findings, especially regarding tumor size and LN metastasis, the 27 patients were divided into groups with different TNM stages (I, $n = 6$; II, $n = 12$; III/IV, $n = 9$). Postoperative RT and CT were performed in seven and three cases, respectively (Table 1).

During the follow-up period, CAC recurrence was found in nine patients — an incidence of 33.3%. The follow-up time ranged from 3 to 107 months, with a mean and median time of 50.26 and 48 months, respectively. The time interval between surgical treatment and CAC relapse was 3–66 months (mean 33.1; median 40). Three cases developed LN ($n = 1$) or lung ($n = 2$) metastasis, with the time interval from treatment completion to distant metastasis being 5, 8, and 20 months, respectively. The three patients died as a result of the lung metastasis ($n = 2$) or natural ageing ($n = 1$).

3.4. Predictors for postoperative recurrence (PC) in Kaplan–Meier and Cox regression analysis

All predictive variables were analyzed to identify their correlation with 5-year recurrence-free survival (RFS) rates for CAC. With Kaplan–Meier analysis, five factors demonstrated a significant association with PC, evidenced by the fact that their p-values were less than 0.05 (Table 1; Fig. 4). Others failed to show a statistical association with PC in univariate analysis. When all factors were further entered into a Cox regression analysis, only three variables maintained their predictive role after eliminating interactions among different parameters. The patients who received a superficial parotidectomy were 0.046 times more likely to develop PC than those who only received enucleation ($p = 0.032$; 95% CI: 0.003–0.070). The probability of PC in patients with the cribriform subtype was 9.701 times that for cases with the papillary pattern ($p = 0.016$; 95% CI: 1.517–62.030). The risk of PC increased abruptly, with an OR of 6.373 ($p = 0.042$; 95% CI: 1.070–37.965), when LN metastasis was found in patients (Table 2).

4. Discussion

Cystadenocarcinoma accounts for 2–5% of all salivary gland (major and minor) malignancies, which indicates that CAC is an extremely rare entity in the oral/maxillofacial region, especially in parotid gland. Hitherto, there have been only two reports on CAC in salivary gland, involving 57 cases (35 in parotid gland) and 65 cases (57 in parotid gland). In both studies, CAC in parotid gland was not separately analyzed, and tumor recurrence and related prognostic factors were not involved (Foss et al., 1996; Cai et al., 2016).

Our study was the first to probe into the postsurgical recurrence (PC) of CAC in parotid gland. Nine of the 27 patients developed local or regional recurrence — an incidence of 33.3%, which was a relative high proportion for parotid gland malignancies. In the study by Cai et al., the recurrence ratio was not ascertained because of data missing from SEER (Cai et al., 2016). Foss et al. found local relapse in three out of 57 patients — a recurrence ratio of 5.3% — with a mean interval of 76 months, and lymph node metastasis in four out of 57 cases — a metastatic ratio of 7.0% (Foss et al., 1996). Mukaigawa et al. reported four CAC cases in parotid gland, submandibular gland, and tongue, and found PC in three — an incidence of over 70%, which was markedly higher than all previous related publications. This can be ascribed to the small sample size (Mukaigawa et al., 2016). The reason why the recurrence incidence for CAC in our study was relatively higher than that found by Cai et al. and Foss et al. can be explained by: 1) preoperative misdiagnosis as benign neoplasms; 2) the therapeutic option of enucleation; and 3) poor biological behavior (Cavalcante et al., 2007).

The therapeutic options for parotid gland tumor comprised enucleation, extracapsular dissection and superficial parotidectomy, and total parotidectomy. Enucleation offers some advantages, including reduced time of operation, a lower risk of facial nerve injury, and restoration of parotid gland function. Some studies have noted that inevitable capsule (pseudo) residue in the surgical site might increase the risk of recurrence (Espinosa et al., 2018). This clinical experience was verified by our data, with cases treated with SP/TP showing a much lower risk of PC compared with those who only received tumor enucleation, according to univariate and multivariate analysis. Based on this finding, enucleation alone should not be advocated when a neoplasm in parotid gland has been preoperatively diagnosed as CAC. Extracapsular dissection and superficial parotidectomy should be the most applied therapeutic options for this rare entity. For those masses involved in the deep lobe of the parotid gland, or presenting with facial nerve injury, TP with or without facial nerve preservation should be the first-choice approach (Colella et al., 2015).

A key point is how to make an accurate preoperative diagnosis, thus prompting the appropriate treatment. Nakazawa et al. performed fine-needle aspiration cytology (FNAC). A cystic neoplasm with uncertain malignancy was preoperatively diagnosed in combination with radiological findings, thus allowing an appropriate therapeutic strategy (Nakazawa et al., 2011). Ko et al. also used fine-needle aspiration cytology to confirmed uncertain malignant potential, based on which extracapsular dissection and superficial parotidectomy were performed, with a final pathological diagnosis of low-grade cribriform CAC (Ko and Koo, 2013). Kawahara et al. also insisted that cytological diagnosis of CAC is very important for

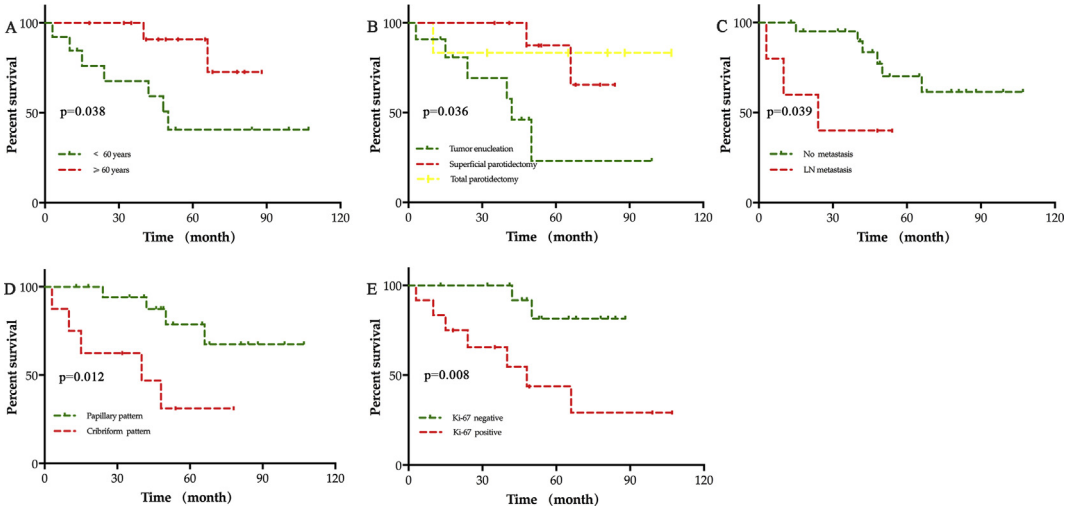

Fig. 4. Recurrence survival curves for CAC patients with statistical significance in Kaplan–Meier analysis: A. age ($p = 0.038$); B. therapeutic selection ($p = 0.036$); C. LN metastasis ($p = 0.039$); D. pathological subtype ($p = 0.012$); E. Ki-67 status ($p = 0.008$).

Table 2
Cox regression model analysis of the prognostic factors for predicting CAC recurrence.

Variable	No. of cases	No. of events	Odds ratio	95% confidence interval	*p*-value
Age (Yr)					
< 60	13	7	Reference		
≥60	14	2	0.134	0.027–1.619	0.134
Treatment					
Tumor enucleation	11	6	Reference		
Superficial parotidectomy	10	2	0.046	0.003–0.770	0.032
Total parotidectomy	6	1	0.818	0.067–9.935	0.875
LN metastasis					
No	22	6	Reference		
Yes	5	3	6.373	1.070–37.965	0.042
Pathological subtype					
Papillary	19	4	Reference		
Cribriform	8	5	9.701	1.517–62.030	0.016
Ki-67 status					
Negative	15	2	Reference		
Positive	12	7	4.031	0.493–33.042	0.194

LN: lymph node.

differential diagnosis between benign and malignant lesions, and that preoperative FNAC should be performed to summarize the cytological features of CAC (Kawahara et al., 2010). In pulmonary mucinous CAC, clinical and radiological examination may show features common to other benign or malignant tumors, preoperative FNAC can distinguish benign neoplasm from malignancies, and the final confirmation should be based on histological observation (Chhieng, 2008). Although it is difficult for FNAC to make a definite diagnosis of this entity, the differential diagnosis between benign and malignant tumors would be of great help to surgeons deciding on whether to perform enucleation, SP, or TP (Aloudah et al., 2009). In conclusion, preoperative fine-needle aspiration can initially help ascertain the benign or malignant status of CAC, thus leading to the appropriate treatment for improving the prognosis of this rare entity. Further studies should focus on correlation analysis of preoperative FNAC with histological diagnosis, thus improving the accuracy of FNAC diagnosis.

The mechanism of lymph node (LN) and distant metastasis is still unclear in CAC patients. Five cases with LN metastasis were found in our study, an incidence of 18.5%. Through SEER database analysis, Cai et al. found four cases with LN metastasis, an incidence of 16%; no distant were was found (Cai et al., 2016). In their study, Foss et al. found an LN metastasis incidence of 7.0% (Foss et al., 1996). Using log-rank and Cox model analyses, we proved the predictive role of LN metastasis on postoperative recurrence of CAC, both in univariate and multivariate analysis. In other words, patients with LN metastasis are more prone to tumor relapse compared with cases with negative LN results. In our cases, the notable finding during follow-up was that two patients developed lung and mediastinum metastases, and both died of lung malignancies at 6 and 18 months after diagnosis of distant metastasis.

The most common subtype of CAC in pathology is papillary pattern, followed by cribriform and mucinous (Doulamis et al., 2016; Harimaya et al., 2006; Michal et al., 2013; Giblett et al., 2017; Wanjari et al., 2014; Takei et al., 2012; Srivanitchapoom et al., 2014; Cavalcante et al., 2007; Nakazawa et al., 2011; Mardi et al., 2010; ÜOzlem et al., 2006; Laco et al., 2010; Nishijima et al., 2017; Wang et al., 2013; Ohta et al., 2016; Arai et al., 2009; Aydin et al., 2005). In our study, 19 cases (70.4%) were diagnosed with papillary pattern and eight (29.6%) with cribriform pattern. Thus far, no investigation has involved a comparison analysis of papillary and cribriform patterns and outcome prediction, especially for local recurrence. Our findings suggested that patients with cribriform pattern were more likely to develop local relapse after surgical procedures. Cribriform pattern is characterized by non-encapsulated, cyctically enlarged ducts with intraductal

proliferation, with typical cysts lined with a layer of small, proliferating ductal cells (Arai et al., 2009). These features may facilitate the invasiveness of CAC.

Ki-67 is a biological marker that serves as an indicator of cell proliferation in tumors, thus estimating the biological activity of neoplasm. Among our pathological slides, 44.4% showed a positive reaction for Ki-67 on immunohistochemical analysis. Ki-67 was positive in all five patients with a different proliferation index (less than 25%) (Laco et al., 2012). In univariate analysis, Ki-67 was an effective predictor for tumor relapse. It lost its predictive role when enrolled into the Cox regression model, but it still has an indicative role for clinical intervention.

5. Conclusion

Papillary cystadenocarcinoma (CAC) is an extremely rare entity in oral, maxillofacial, or head and neck regions. Through a case review, we found that CAC has no specific clinical manifestations, allowing it to be easily misdiagnosed as other common neoplasms of parotid gland. It is difficult to make an accurate preoperative diagnosis of CAC, but fine needle aspiration can be used as a preliminary method to assess the status (benign or malignant), thus suggesting appropriate therapeutic strategies. CAC patients with LN metastasis, cribriform pattern, and Ki-67 positivity, should be treated further to avoid tumor relapse.

There were several limitations in this study. First, it is difficult to entirely eliminate selection and document bias in a retrospective study, and unknown confounding variables may affect the statistical results. Second, four patients were not included on the basis of the exclusion criteria. These missing data could cause statistical bias and reduce the power of statistical significance. Third, results collated from single institutions are less powerful than those from multicenter investigations.

Funding disclosure

None.

Conflicts of interest

None declared.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcms.2019.02.005.

References

Aloudah NM, Raddaoui E, Aldhahri S, Al-Abbadi MA: Low-grade papillary cystadenocarcinoma of the parotid gland: presentation of a case with cytological, histopathological, and immunohistochemical features and pertinent literature review. Diagn Cytopathol 37(2): 128–131, 2009

Arai A, Taki M, Mimaki S, Ueda M, Hori S: Low-grade cribriform cystadenocarcinoma of the parotid gland: a case report. Auris Nasus Larynx 36(6): 725–728, 2009

Aydin E, Turkoglu S, Ozen O, Akkuzu B: Mucinous cystadenocarcinoma of a minor salivary gland in the upper lip: case report. Auris Nasus Larynx 32(3): 301–304, 2005

Cai CF, Sun JY, He ZY, Lin HX, Liu FR, Wang Y: Clinicopathological characteristics, treatment, and survival outcomes of cystadenocarcinoma of the salivary gland: a population-based study. OncoTargets Ther 9, 2016 6569–72

Cavalcante RB, da Costa Miguel MC, Souza Carvalho AC, Maia Nogueira RL, Batista de Souza L: Papillary cystadenocarcinoma: report of a case of high-grade histopathologic malignancy. Auris Nasus Larynx 34(2): 259–262, 2007

Chhieng DC: Fine-needle aspiration cytology of pulmonary mucinous cystadenocarcinoma. Diagn Cytopathol 36(8): 581–585, 2008

Colella G, Cannavale R, Chiodini P: Meta-analysis of surgical approaches to the treatment of parotid pleomorphic adenomas and recurrence rates. J Craniomaxillofac Surg 43(6): 738–745, 2015

Doulamis IP, Mylonas KS, Kalfountzos CE, Mou D, Haj-Ibrahim H, Nasioudis D: Pancreatic mucinous cystadenocarcinoma: epidemiology and outcomes. Int J Surg 35: 76–82, 2016

Espinosa CA, Fernández-Valle Á, Lequerica-Fernández P, de Villalaín L, de Vicente JC: Clinicopathologic and surgical study of pleomorphic adenoma of the parotid gland: analysis of risk factors for recurrence and facial nerve dysfunction. J Oral Maxillofac Surg 76(2): 347–354, 2018

Foss RD, Ellis GL, Auclair PL: Salivary gland cystadenocarcinomas. A clinicopathologic study of 57 cases. Am J Surg Pathol 20(12): 1440–1447, 1996

Giblett N, Ahsan SF, Messahel A: Papillary cystadenocarcinoma of the sublingual gland. J Oral Biol Craniofac Res 7(3): 223–225, 2017

Harimaya A, Somekawa Y, Sasaki M, Ohuchi T: Cystadenocarcinoma (papillary cystadenocarcinoma) of the submandibular gland. J Laryngol Otol 120(12): 1077–1080, 2006

Kawahara A, Harada H, Mihashi H, Akiba J, Kage M: Cytological features of cystadenocarcinoma in cyst fluid of the parotid gland: diagnostic pitfalls and literature review. Diagn Cytopathol 38(5): 377–381, 2010

Ko YS, Koo JS: Cytomorphological findings and histological correlation of low-grade cribriform cystadenocarcinoma of salivary gland in fine-needle aspiration: a case study. Korean J Pathol 47(6): 592–595, 2013

Kokabu S, Nojima J, Kayano H, Yoda T: Low-grade cribriform cystadenocarcinoma of the palatal gland: a case report. Oncol Lett 10(4): 2453–2457, 2015

Koufopoulos N, Goudeli C, Syrios J, Filopoulos E, Khaldi L: Mucinous cystadenocarcinoma of the breast: the challenge of diagnosing a rare entity. Rare Tumors 9(3): 7016, 2017

Laco J, Podhola M, Dolezalova H: Low-grade cribriform cystadenocarcinoma of the parotid gland: a neoplasm with favorable prognosis, distinct from salivary duct carcinoma. Int J Surg Pathol 18(5): 369–373, 2010

Laco J, Kamarádová K, Vítková P, Sehnálková E, Dvořáková S, Václavíková E, et al: Cribriform adenocarcinoma of minor salivary glands may express galectin-3, cytokeratin 19, and HBME-1 and contains polymorphisms of RET and H-RAS proto-oncogenes. Virchows Arch 461(5): 531–540, 2012

Mardi K, Sharma S, Gupta N: Papillary cystadenocarcinoma of submandibular salivary gland: a rare case report. J Cancer Res Ther 6(3): 330–332, 2010

Michal M, Kacerovska D, Kazakov DV: Cribriform adenocarcinoma of the tongue and minor salivary glands: a review. Head Neck Pathol 7(Suppl. 1), 2013 S3–11

Mukaigawa T, Hayashi R, Miyazaki M, Shinozaki T, Tomioka T, Fujii S: Cystadenocarcinoma of the salivary glands with potential lymph node metastasis. Auris Nasus Larynx 43(3): 340–344, 2016

Nakagawa T, Hattori K, Iwata N, Tsujimura T: Papillary cystadenocarcinoma arising from minor salivary glands in the anterior portion of the tongue: a case report. Auris Nasus Larynx 29(1): 87–90, 2002

Nakazawa T, Kondo T, Yuminomochi T, Nakazawa K, Ishii Y, Mochizuki K, et al: Fine-needle aspiration biopsy of low-grade cribriform cystadenocarcinoma of the salivary gland. Diagn Cytopathol 39(3): 218–222, 2011

Nishijima T, Yamamoto H, Nakano T, Hatanaka Y, Taguchi KI, Masuda M, et al: Low-grade intraductal carcinoma (low-grade cribriform cystadenocarcinoma) with tumor-associated lymphoid proliferation of parotid gland. Pathol Res Pract 213(6): 706–709, 2017

Ohta Y, Hirota Y, Kohno Y, Kishimoto K, Norose T, Ohike N, et al: Cytology of low-grade cribriform cystadenocarcinoma in salivary glands: cytological and immunohistochemical distinctions from other salivary gland neoplasms. Diagn Cytopathol 44(3): 41–45, 2016

Seifert G, Sobin LH (eds), Histological typing of salivary gland tumours, 2nd ed. Berlin: Springer-Verlag, 1991

Shannon VR, Nanda AS, Middleton LP, Faiz SA: Pulmonary mucinous cystadenocarcinoma presenting as extensive multifocal cystic lesions. Am J Respir Crit Care Med 195(9): 1267–1268, 2017

Srivanitchapoom C, Sittitrai P, Mahanupab P: Central papillary cystadenocarcinoma of the mandible: a case report and review of the literature. Int J Surg Case Rep 5(6): 330–334, 2014

Takei R, Tomihara NA, Noguchi M: Central cystadenocarcinoma of the mandible. Int J Oral Maxillofac Surg 41(12): 1463–1466, 2012

Ü Murat, Ozlem A, Yucel A, Yavuz SP, Tugay C: Papillary cystadenocarcinoma of the submandibular gland. Oral Oncol Extra 42(2): 82–84, 2006

Wang L, Liu Y, Lin X, Zhang D, Li Q, Qiu X, et al: Low-grade cribriform cystadenocarcinoma of salivary glands: report of two cases and review of the literature. Diagn Pathol 8(28), 2013

Wanjari SP, Wanjari PV, Patidar KA, Parwani RN: Papillary cystadenocarcinoma of the hard palate. BMJ Case Rep 2014, 2014